

REMARKS

Claims 1, 3-21, and 25-41 are pending in this application, with the addition of new claim 41. New claim 41 is supported by claims 1, 2, and 22-24 as originally filed, by Example 1, pages 23-28, and by page 4, lines 19-21, of the specification. The amendments to claim 1 are supported by the claims as originally filed and on page 7, lines 16-20, of the specification. These amendments highlight the features of the claimed invention and do not add new matter. The amendment to claim 14 merely corrects a typographical error and does not add new matter.

Applicants note that the Office has entered the submission filed November 16, 2005, which was an Amendment presented with a Request for Continued Examination. There is no indication that the Supplemental Amendment filed December 19, 2005, was entered, though. Applicants have attached Exhibit A, including a copy of the Supplemental Amendment and the receipt postcard, stamped by the Office, as proof of this filing. Applicants request that the Office acknowledge entry of it.

The Office has maintained rejections under 35 U.S. C. § 102 and § 103 in light of WO 95/13799 because it asserts that this reference "teaches a process for microencapsulating an active agent by coacervation" Office Action of December 13, 2005, at 2. The Office continues by comparing the claimed process to that allegedly disclosed in WO 95/13799, finding that the reference anticipates or renders obvious the claimed invention.

As explained in the instant specification, the claimed invention

proposes a process of microencapsulation by coacervation that **does not use any chlorinated solvent**. More specifically, the invention relates to a process of coacervation by addition of nonsolvent. Coacervation by addition of nonsolvent requires the use of three **miscible**

solvents; one of these three solvents is a solvent for the polymer and the other two are nonsolvents for the polymer.

Specification at p. 4, lines 19-27. This aspect of the invention is important because it provides a solution for the need in the art for encapsulation methods that are not neurotoxic due to chlorinated solvent. See specification at p. 3, lines 10-24. Thus, independent claims 1 and 41 are drawn to processes of coacervation “wherein the non-solvent . . . is **miscible** with said organic solvent for the polymer . . .”, and claim 41, specifically recites that “microencapsulating the active principle by coacervation does not use an chlorinated solvent.”

The Office acknowledged the immiscibility of the phases described in WO 95/13799, but seemed to give this feature consideration only in the context of Applicants’ previous argument about use of a mixer, see Office Action at p. 4, item 7 (“Applicants argue that since the WO ‘799 reference discloses the use of a mixer to mix the first and second phases, these solutions are immiscible.”). That the disclosure of WO 95/13799 extends only to immiscible phases is apparent from its text, though. For example, on page 8, lines 10-11, the text of WO 95/13799 provides “the first phase and the second phase are substantially **immiscible**.” (emphasis added); see *also* p. 10, lines 23-24, and p. 11, lines 2-3. This “first phase” is analogous to the phase of the instant invention comprising the organic solvent for the polymer (“the solvent”), the polymer dissolved therein, and the active principle, see WO 95/13799 at p. 8, lines 7-8, and the “second phase” is analogous to the non-solvent of the instant invention because it is “free from solvents for the polymer and active agent,” see *id.* at p. 8, lines 12-13. Thus, while the analogous phases are immiscible in WO 95/13799, they are miscible in the instant invention.

The Office rejected Applicants' previous argument that the process disclosed in WO 95/13799 differs from the claimed invention because WO 95/13799 teaches the use of silicone oil as a non-solvent. The Office asserted that this distinction is not convincing because of the composition of the "solvent blend" disclosed in WO 95/13799. But this "solvent blend" does not correlate with the "non-solvent" of the claimed invention and, therefore, indicates nothing about anticipation or obviousness of the claimed invention. In fact, silicone oil is mentioned in the instant specification only in regard to prior art coacervating agents, see specification at p. 7, lines 22-25, or for stabilization to prevent aggregation of particles, see *id.* at p. 6, lines 7-20. Thus, the use of silicone oil as a non-solvent in WO 95/13799 distinguishes the process disclosed in this reference from the claimed invention.

In general, WO 95/13799 does not disclose the same process as that claimed here. WO 95/13799 teaches a process for encapsulating active agents to form controlled-release microparticules through the use of static mixers. The process can be carried out for a variety of techniques used to encapsulate active agents, such as by 1) a phase separation technique or 2) a solvent extraction technique. See WO 95/13799 at page 8, lines 14-16, and page 29, lines 4-9.

Discussion of phase separation techniques, also called "non-solvent induced coacervation," can be found on page 5, line 9, through page 6, line 2, on page 29, lines 4-17, and in Examples 11-14 of WO 95/13799. But each of these passages teach a limited set of reagents, wherein silicon oil is the only non-solvent, ethyl acetate is the only solvent, and heptane is the only curing agent disclosed. WO 95/13799 does not disclose the non-solvent/curing agents recited in claims 1 and 41 and these claimed

reagents differ significantly in their chemical properties from silicone oil as the nonsolvent, ethyl acetate as the solvent, and heptane as the curing agent. For example, silicon oils are comprised of a chain of polydimethylsiloxane (PDMS), but the non-solvents of the claimed invention are selected from alcohols or ketones containing 2 to 3 carbon atoms. Furthermore, heptane is an alkane containing seven carbon atoms, but the curing agents of the claimed invention are selected from water or an alcohol containing 1 to 4 carbon atoms. Thus, because of the differences in the reagents disclosed, the solvent extraction technique of WO 95/13799 does not anticipate the claimed invention, nor does it render it obvious.

Similarly, the other technique disclosed in WO 95/13799, the solvent extraction technique, does not anticipate or render the claimed invention obvious. The disclosure of this technique in WO 95/13799 implies the use of at least two **immiscible** solvents, which form an emulsion when combined together, see WO 95/13799 at page 8, line 10-11; page 10, lines 23-24; and page 11, lines 2-3, while the claimed invention requires a solvent that is **miscible** with a non-solvent.

The solvent extraction technique (called "emulsion-extraction" or "emulsion-evaporation" in the present specification, see specification at page 2, lines 24-17) also differs from the claimed invention, which relies on a phase separation technique (coacervation). See instant specification at p. 1, lines 5-6 ("The present invention relates to a process for microencapsulating an active principle by coacervation . . .").

Exhibit B provides a schematic explanation of differences between the claimed invention and that disclosed in WO 95/13799. Briefly, in the claimed invention coacervation is induced by the addition of the nonsolvent to the phase, which contains

the solvent, the polymer, and the active agent. The result is **one liquid phase** through which is dispersed pre-formed solid microparticles of polymer containing the active agent. The polymer is not dissolved in the liquid phase because the liquid phase contains the nonsolvent for the polymer. Instead, it is deposited at the surface of the active agent. The last step of the process is the curing of the pre-formed microparticles with the curing agent.

In contrast, according to the solvent extraction technique of WO 95/13799, an emulsion is formed between the first phase and the second phase. The result is **two liquid phases** immiscible one to each other, one continuous and the other one discontinuous. The discontinuous phase comprising liquid droplets, which are composed of the initial first phase, containing the "solvent blend", the polymer dissolved therein, and the active agent. The polymer is not solid because it is dissolved in the droplets of the solvent blend. Thereafter, an aqueous extraction of the solvent is performed with the quench liquid in order to remove the solvent from the droplets and to recover the microparticles. See WO 95/13799 at p. 9, lines 14-29, and p. 10, lines 1-19.

Because the claimed invention does not involve an emulsion, but emulsions are formed in the process described in WO 95/13799, the disclosure of a solvent extraction technique in WO 95/13799 does not anticipate or render obvious the claimed invention, either inherently or expressly.

In conclusion, WO 05/13799 does not disclose a process for microencapsulation with a non-solvent that is miscible with an organic solvent and with the particular claimed solvents, non-solvents, and curing agents. Without disclosing these elements, WO 05/13799 cannot anticipate the invention claimed in claims 1 and 41, or the claims

that depend on them, nor can it render them obvious. Accordingly, Applicants request that the rejections in light of WO 95/13779 be withdrawn and claims 1, 3-21, and 25-41 be allowed.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: May 11, 2006

By: 

Deborah Katz

Reg. No. 51,863

Phone: 202-408-4382

Fax: 202-408-4400

Email: deborah.katz@finnegan.com

Attachments:

Exhibit A: a copy of the Supplemental Amendment filed December 19, 2005, and the accompanying stamped receipt postcard;

Exhibit B: Figure